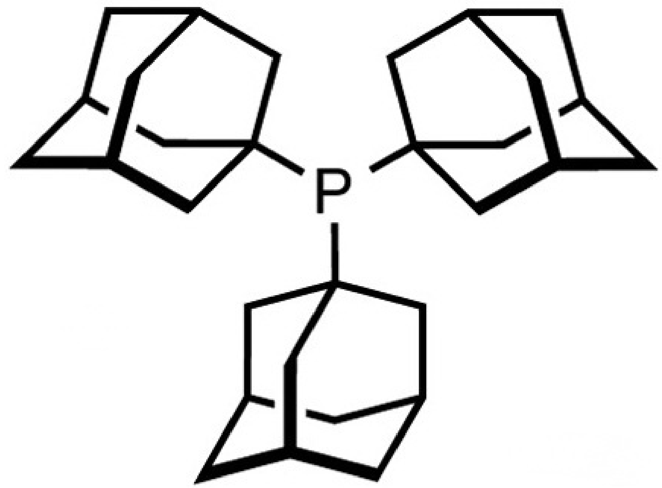
*tri*Diamondoidphosphine Ligands
for Palladium-catalyzed Cross Coupling Reactions

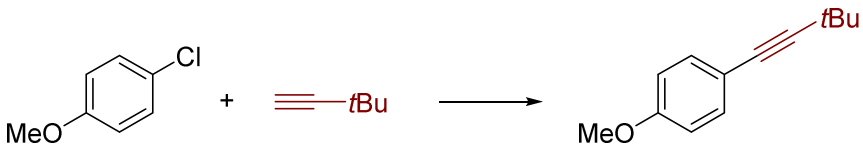
Seminar talk presented by
Dr. Boryslav Tkachenko



August 18th, 2017

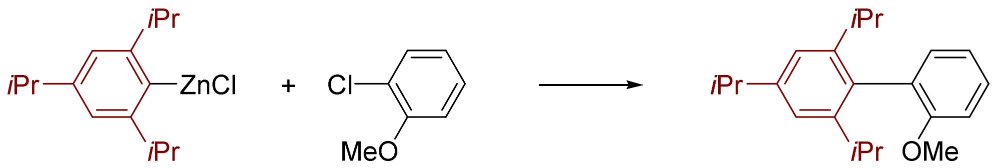
AG Schreiner
Institute of Organic Chemistry
Justus-Liebig University Giessen

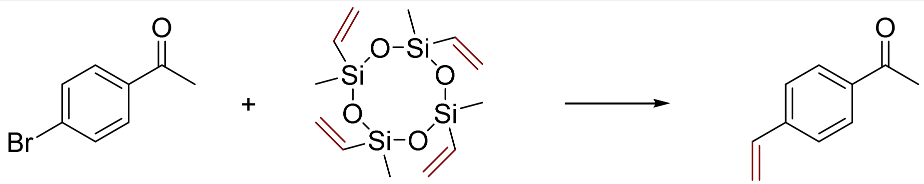
Examples of Palladium Catalyzed Cross-coupling Reactions



Sonogashira

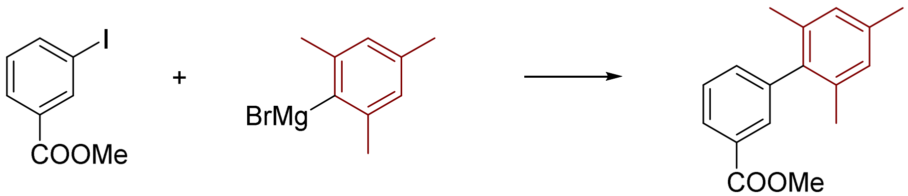
Negishi

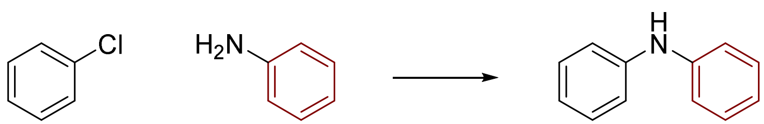




Hiyama

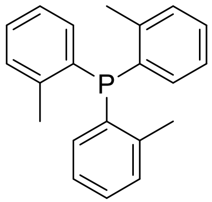
Kumada



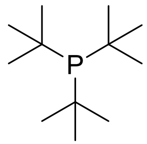


Buchwald-Hartwig
Amination

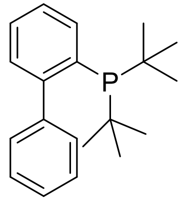
Hindered Phosphines as Active Catalysts for Cross-coupling Reactions



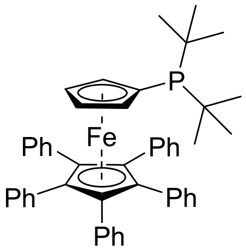
Heck
(1978)



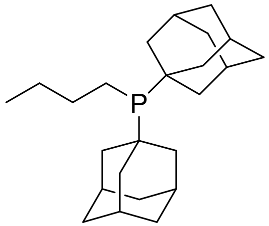
Fu, Koie, Hartwig
(1998-1999)



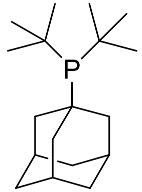
Buchwald
(1999)



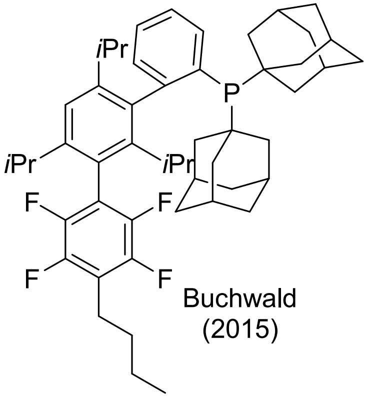
Hartwig
(2000)



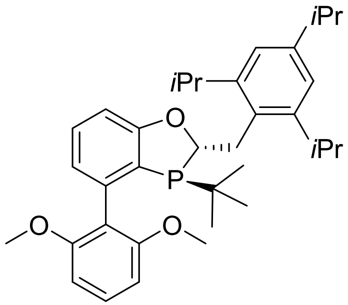
Beller
(2000)



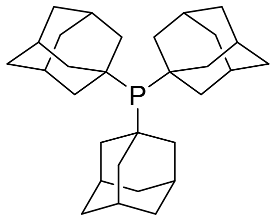
Hartwig
(2001)



Buchwald
(2015)



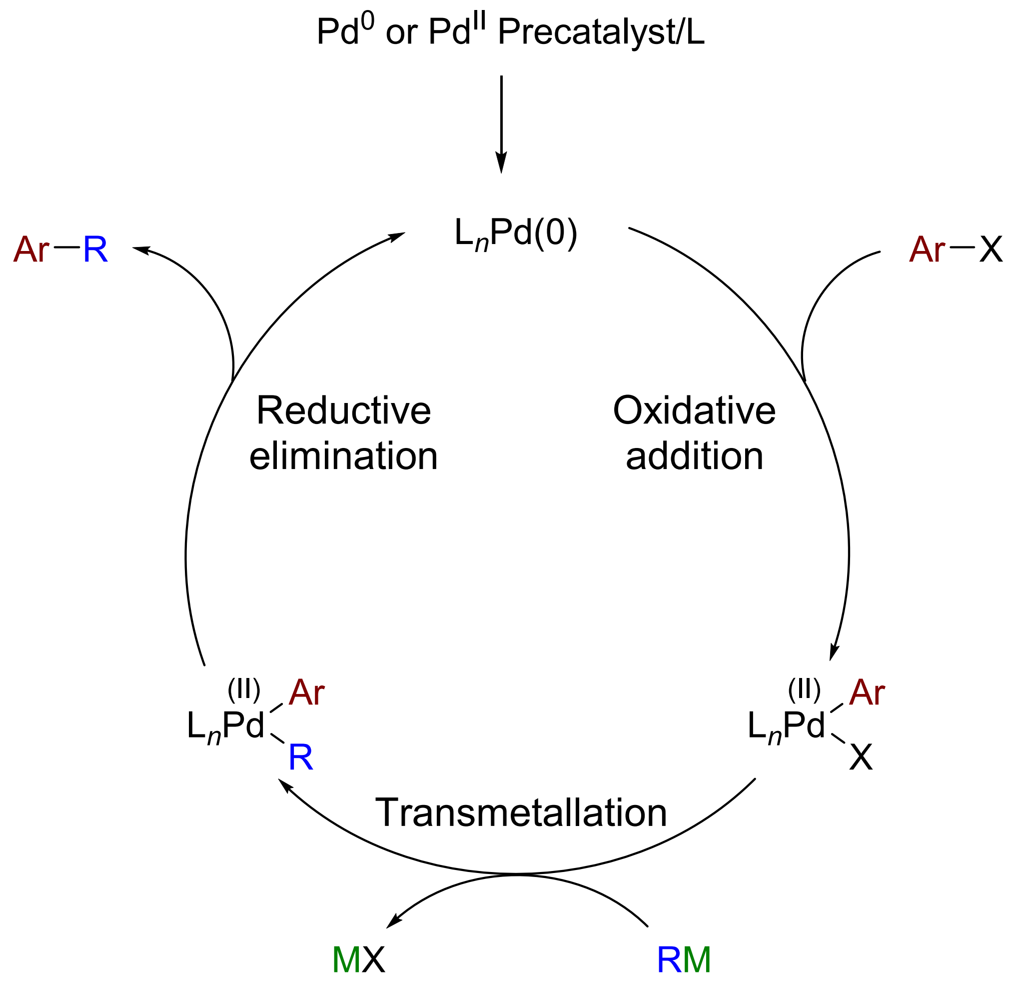
Lipshutz
(2016)



Carrow
(2016)

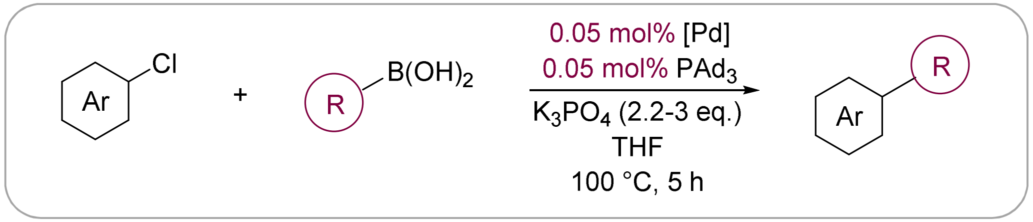
B. P. Carrow, L. Chen *Synlett* **2017**, *13*, 280-288.

General Mechanism for Palladium-catalyzed Cross Coupling Reactions

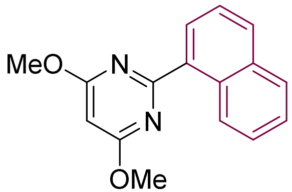


C. A. Fleckenstein, H. Plenio *Chem. Soc. Rev.* **2010**, *39*, 694-711.

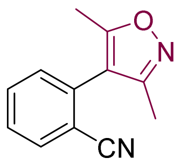
Examples of Suzuki–Miyaura Coupling with Challenging Substrate Classes and a PAd_3-Pd Catalyst



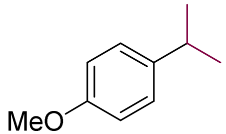
Chloroheteroarenes | Hindered Biaryls | $C(sp^2)$--$C(sp^3)$ | o-Fluorinated and 2-Heteroaryl Boronic Acids



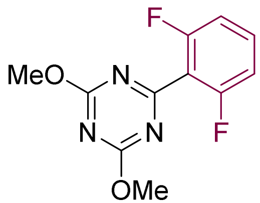
80%
(0.005 mol% [Pd])
TON 16000



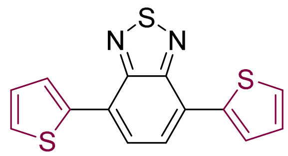
79% (9 h)



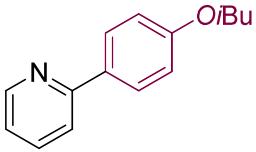
70%
(1 mol% [Pd])



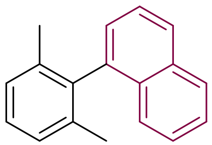
93%
(0.1 mol% [Pd], RT)



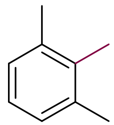
95% (RT, 1 h)



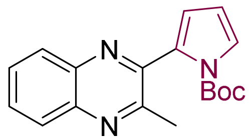
74%
(1 h, 0.005 mol% [Pd])
TON 14800



80%



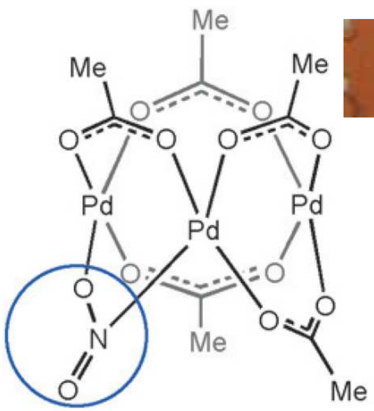
90% (50 °C)



96%
(70 °C)

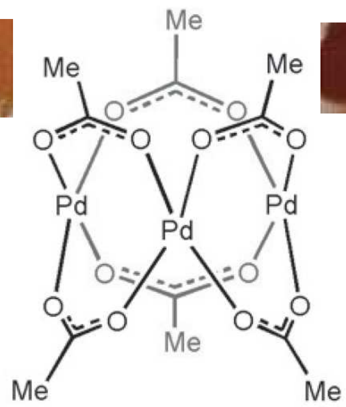
B. P. Carrow, L. Chen *Synlett* **2017**, *13*, 280-288.

$$3Pd + 6HNO_3 + 6HOAc = Pd_3(OAc)_6 + 6NO_2 + 6H_2O$$



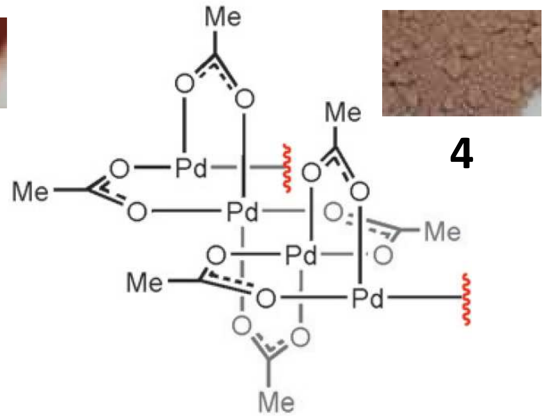

3

$Pd_3(OAc)_5(NO_2)$




2

$Pd_3(OAc)_6$



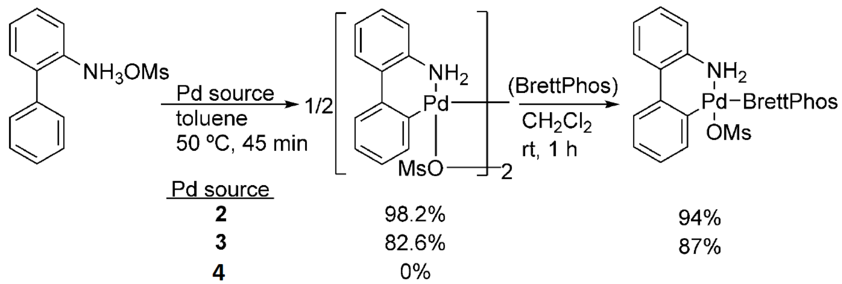
4

$[Pd(OAc)_2]_n$

Melting point and solubility data

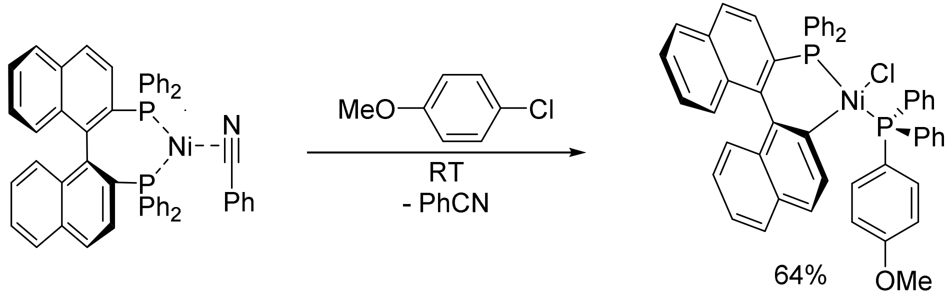
	Decomp range [°C][a]	Solubility [mg mL^{-1}] toluene	acetone	THF	DMF
2	203–205	13.2	19.2	20.0	41.7
3	222–228	13.9	25.0	71.4	100
4	222–224	insol.	insol.	insol.	insol.

Synthesis of 3d-gen. BrettPhos palladacycle

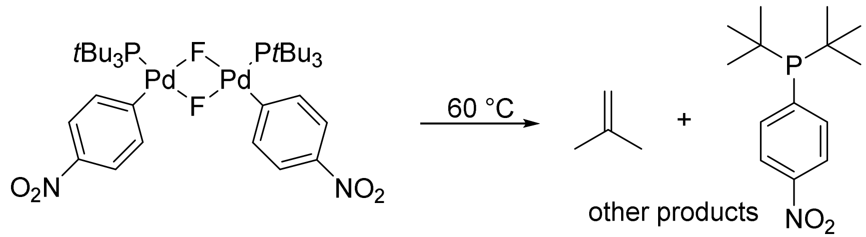


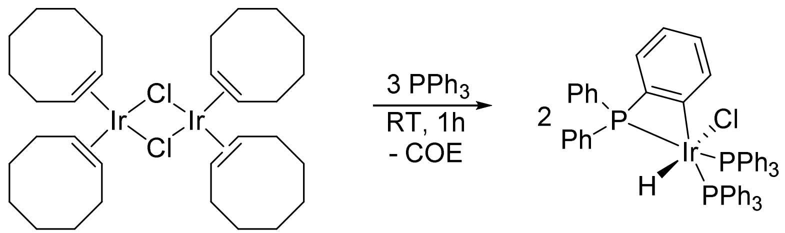
W. A. Carole, T. J. Colacot *Chem.–Eur. J.* **2016**, *22*, 7686-7695.

Side Reactions Representative to Catalyst Deactivation

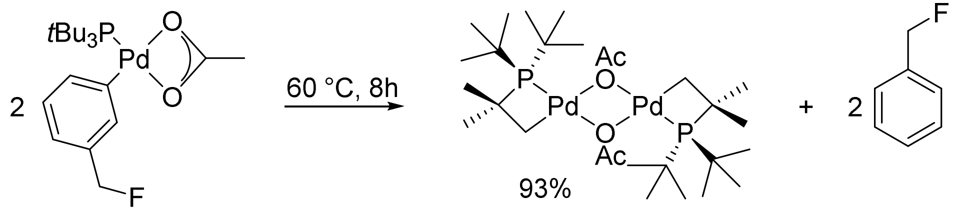


P–C bond cleavage





Cyclometallation

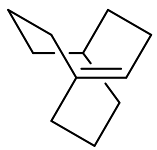


a) S. Ge, R. A. Green, J. F. Hartwig *J. Am. Chem. Soc.* **2014**, *136*, 1617-1627, b) D. V. Yandulov, N. T. Tran *J. Am. Chem. Soc.* **2007**, *129*, 1342-1358,
c) M. Albrecht *Chem. Rev.* **2010**, *110*, 576-623.

The terminus of a double bond cannot exist at the bridgehead position (branching position) of a bridged bicyclic system. *Bredt* ***1924***

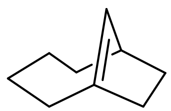
The S value is the sum of atoms contained in all the bridges of the bicyclic system.
Bridged bicyclic systems with bridgehead double bonds with:
S = 9 (8) have the potential to be isolated
S = 7 could be observed but not isolated
S = 6 could be entertained as fleeting intermediates *Fawcett* ***1950***

Isolable



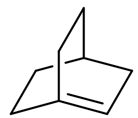
OS ≤ 17 kcal·mol^{-1}
Bicyclo[3.3.3]undec-1-ene

Observable



17 kcal·mol^{-1} ≤ OS ≤ 21 kcal·mol^{-1}
Bicyclo[4.2.1]non-1(9)-ene

Unstable

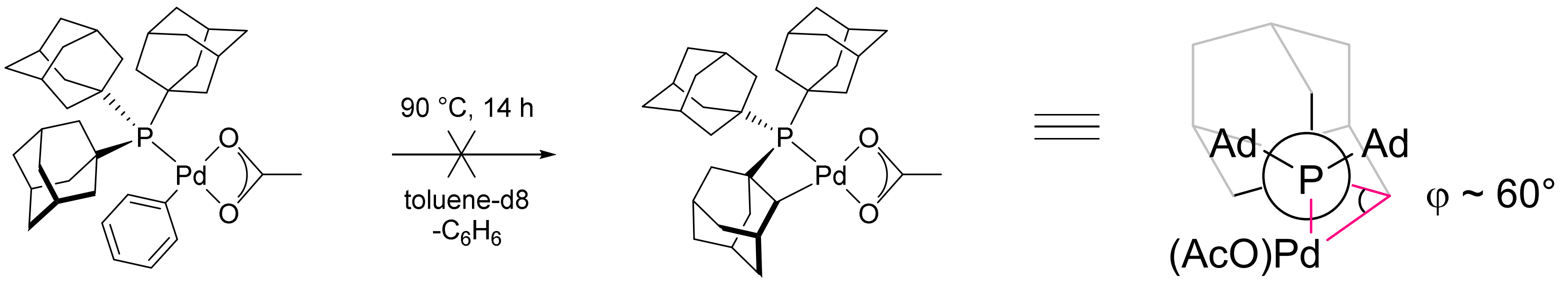


OS ≥ 21 kcal·mol^{-1}
Bicyclo[2.2.2]oct-1-ene

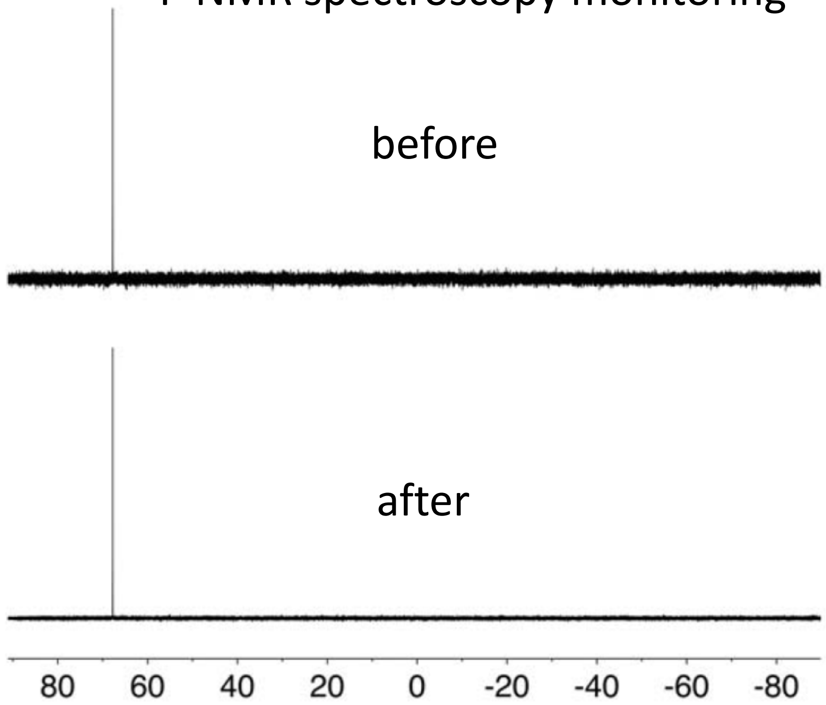
P. v. R. Schleyer ***1979***

J. Bredt *Liebigs Ann. Chem.* **1924**, *437*, 1 – 13;
F. S. Fawcett *Chem. Rev.* **1950**, *47*, 219 – 274;
D. J. Martella, M. Jones, Jr., P. v. R. Schleyer, W. F. Maier *J. Am. Chem. Soc.* **1979**, *101*, 7634 – 7637.

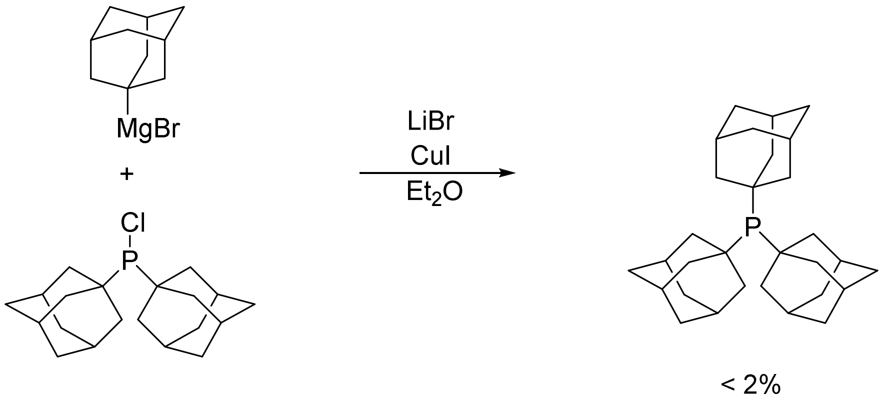
Attempted Cyclometallation of $(PAd_3)Pd(Ph)(\kappa^2\text{-}OAc)$

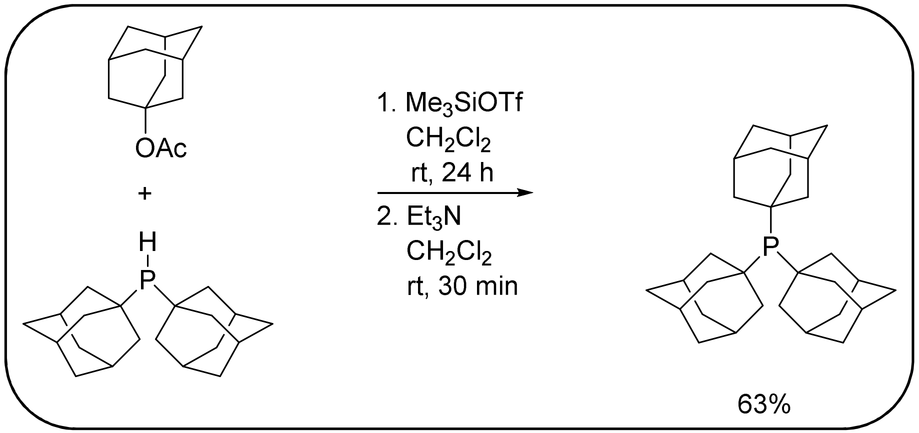


^{31}P NMR spectroscopy monitoring



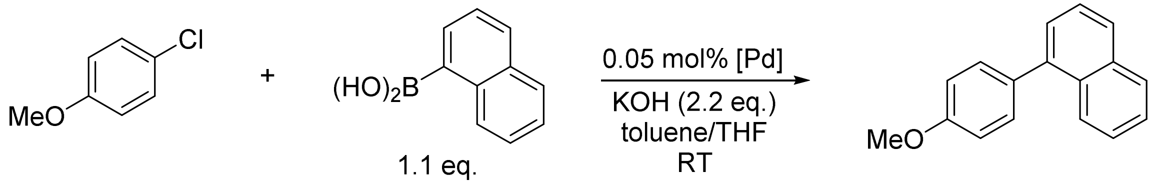
L. Chen, P. Ren, B. P. Carrow *J. Am. Chem. Soc.* **2016**, *138*, 6392-6395.

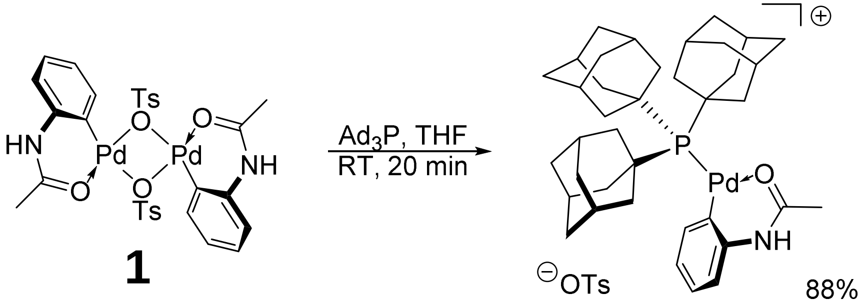




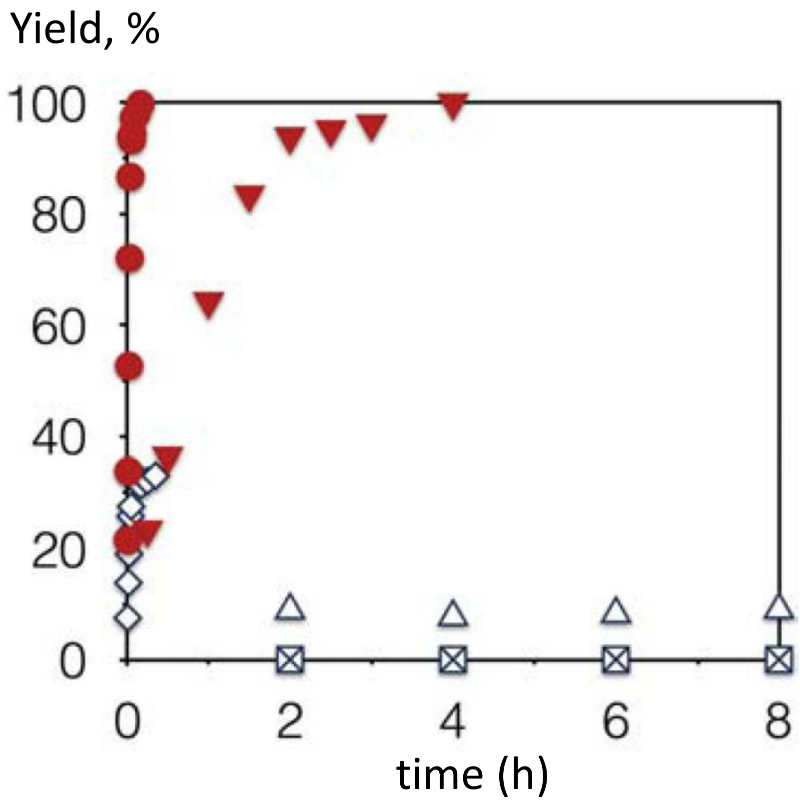
Chen, L.; Ren, P.; Carrow, B. P. *J. Am. Chem. Soc.* **2016**, *138*, 6392-5.

Example of Suzuki–Miyaura Crosscoupling with Chloroarene





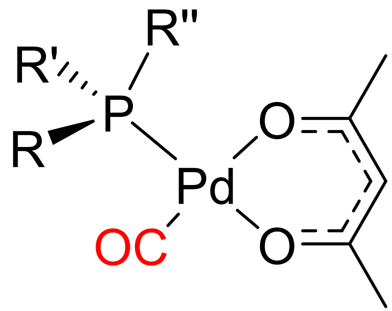
- ● **1** + PAd_3 (0.5 mol%)
- ▼ **1** + PAd_3 (0.05 mol%)
- ◇ **1** + P*t*Bu_3 (0.5 mol%)
- △ **1** + P*t*Bu_3 (0.05 mol%)
- × **1** + PAd_2Bu (0.05 mol%)
- □ **1** + PCy_3 (0.05 mol%)



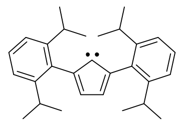
Pd – phosphine complex	**computed cone angle / °**	
	Allen[1] method	**Mingos[2] method**
Pd–PMe_3	120.2	113.6
Pd–P(*t*Bu)$_3$	186.8	178.2
Pd–PAd_3	188.0	179.3
Pd–PAd_2Diam	188.0	179.2
Pd–PAdDiam$_2$	187.9	179.1
Pd–PDiam$_3$	187.8	179.1
Pd–$PHAd_2$	174.4	141.9
Pd–PHDiam$_2$	174.2	141.9

B3LYP-D3/6-31G(d,p) with an effective core potential (LANL2DZ) for the Pd

[1] J. A. Bilbrey, A. H. Kazez, J. Locklin, W. D. Allen *J. Comput. Chem.* **2013**, *34*, 1189,
[2] T. E. Müller, D. M. P. Mingos *Transition Met. Chem.* **1995**, *20*, 533.

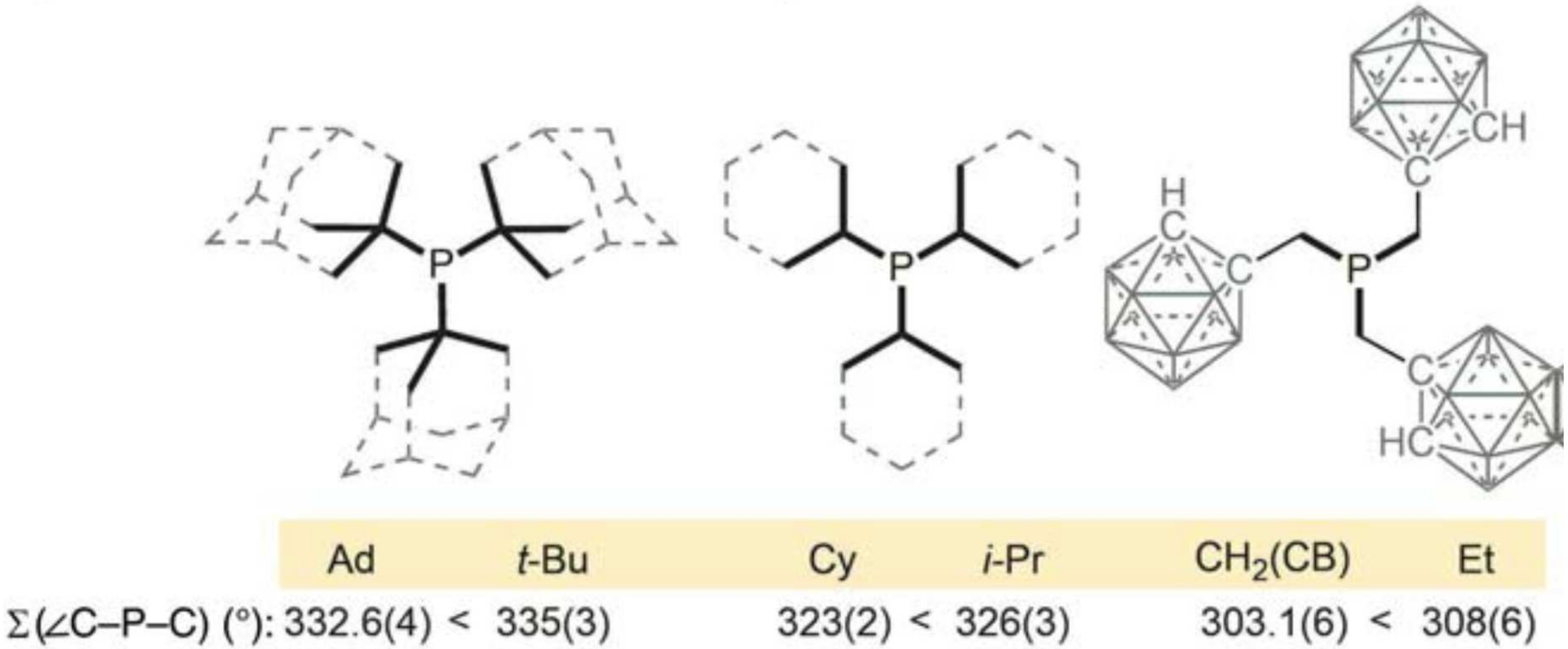


Ligand	$\nu_{CO}(cm^{-1})$
IPr	1963
$PAd_2(n\text{Bu})$	1956.9
$Pt\text{Bu}_3$	1956.4
PAd_3	1948.3



B. P. Carrow, L. Chen *Synlett* **2017**, *13*, 280-288.

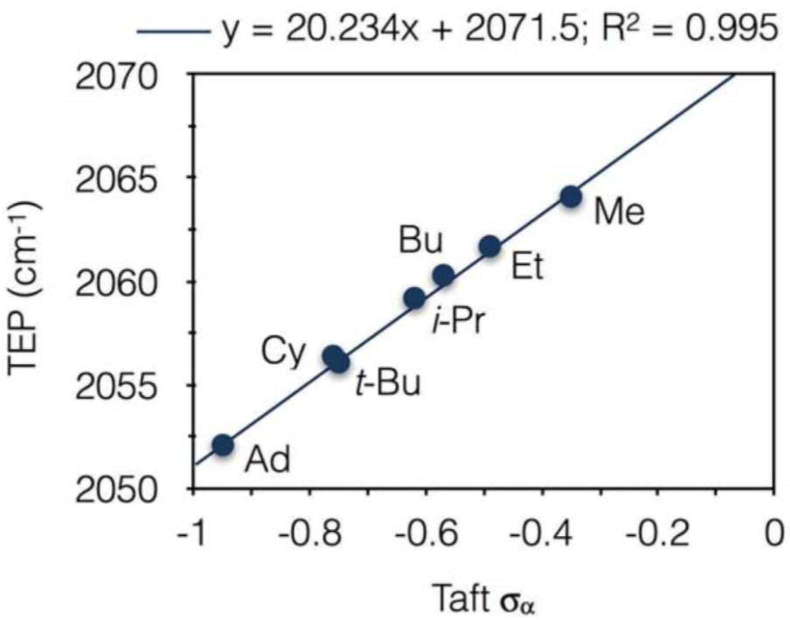
Bent's rule:
Atomic s character concentrates in orbitals directed toward electropositive substituents



CB = 1,2-dicarba-*closo*-dodecaboran-1-yl, $C_2B_{10}H_{11}$

B. P. Carrow, L. Chen *Synlett* **2017**, *13*, 280-288.

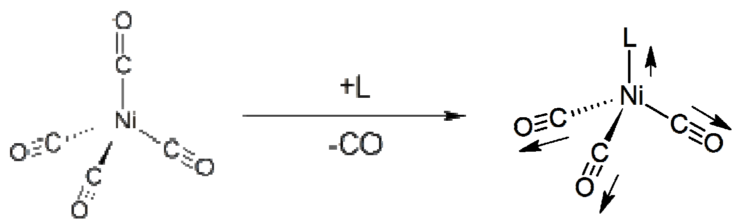
Dependence of Tolman electronic parameter (TEP) on Taft polarizability parameter (σ_α)



The larger Taft polarizability parameter (σ_α) of Ad (−0.95) compared to *t*Bu (−0.75) indicates the former is better able to facilitate electron donation from phosphorus by stabilizing a more polarized P−M dative bond.

Tolman electronic parameter (TEP)

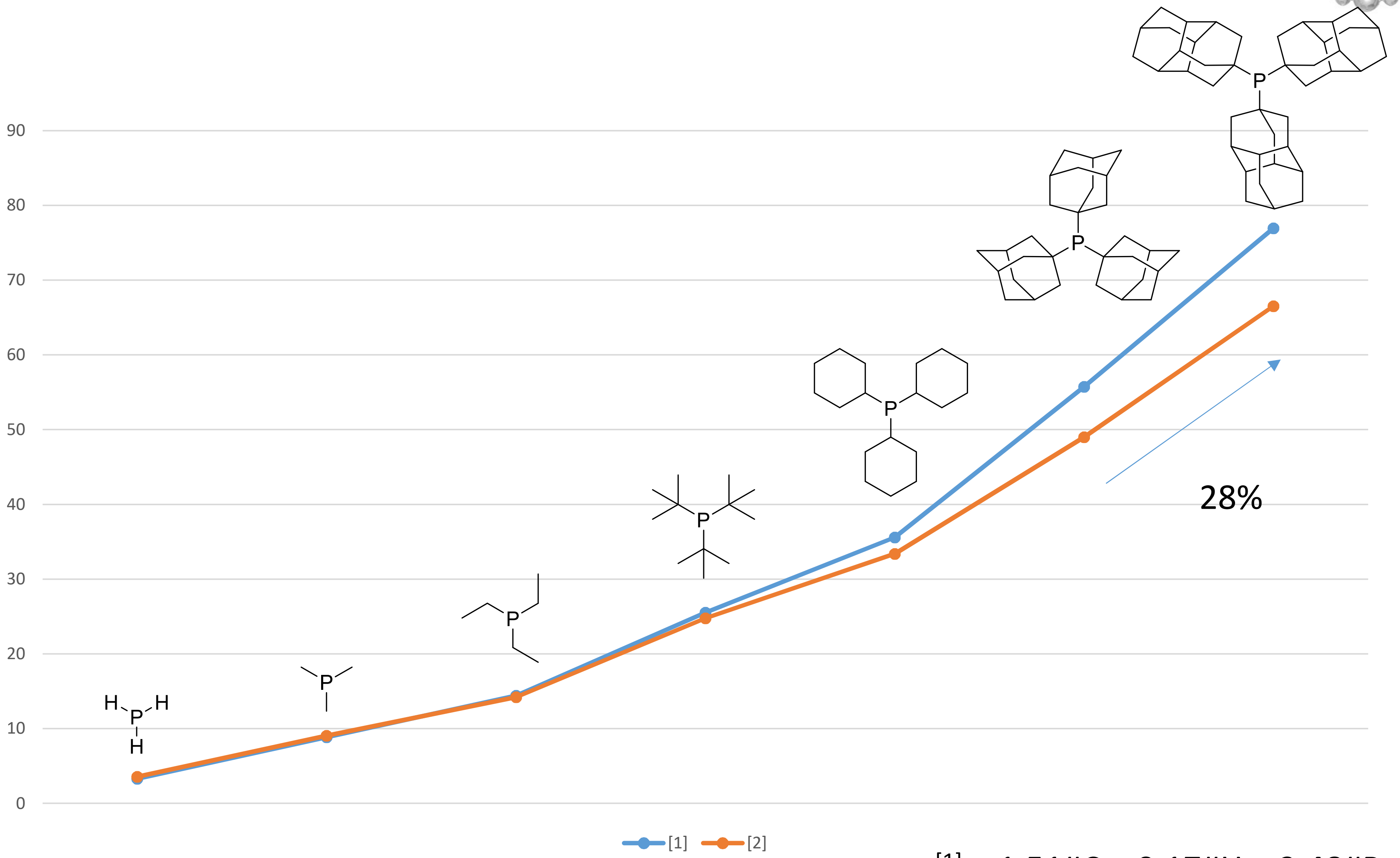
as a measure of the electron donating or withdrawing ability of a ligand



frequency of the A_1 C-O vibrational mode of $LNi(CO)_3$

B. P. Carrow, L. Chen *Synlett* **2017**, *13*, 280-288.

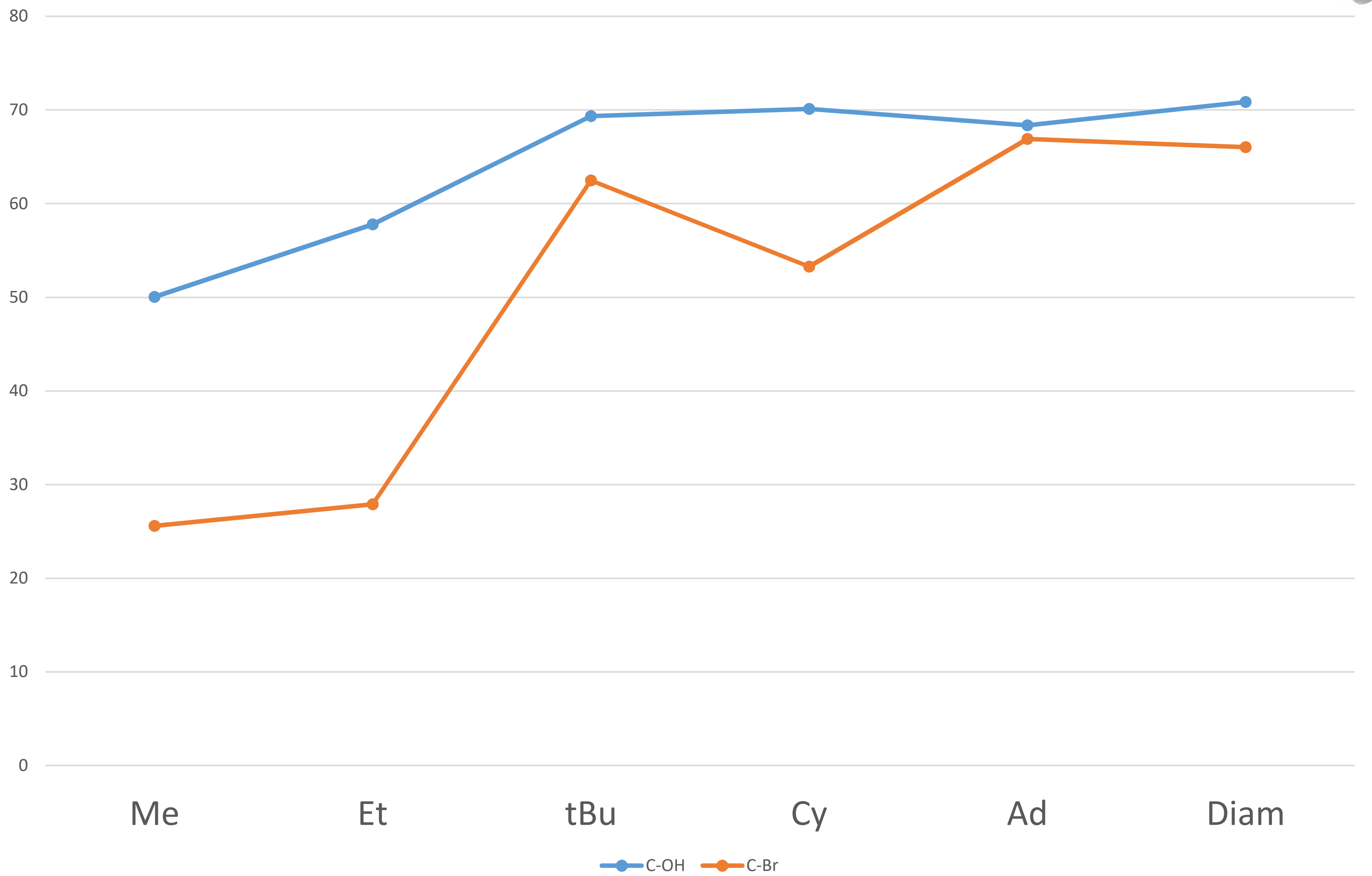
Computed Polarizabilities (Å³) of Phosphines Bearing Various Alkyl Substituents



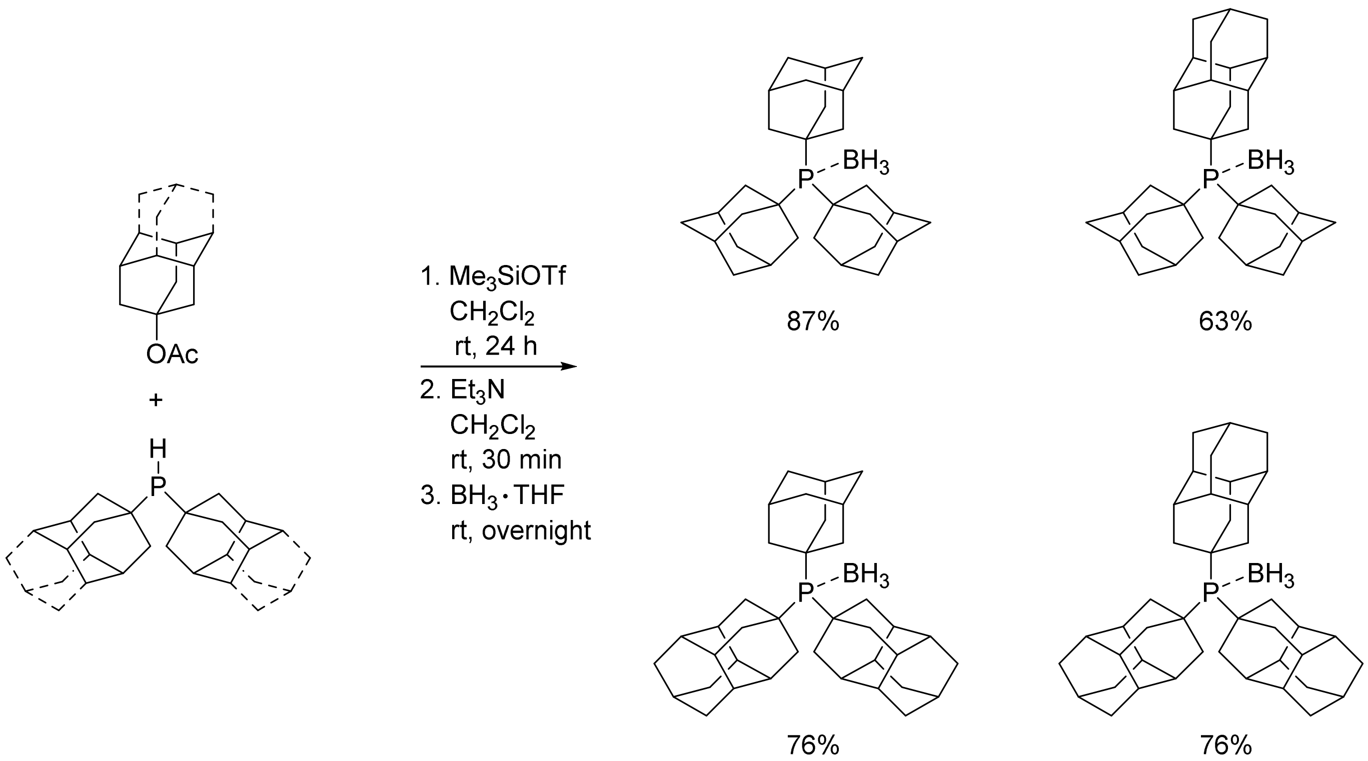
$\alpha_{calc}^{[1]} = 1.51\#C + 0.17\#H + 2.48\#P$

[1] R. Bosque, J. Sales *J. Chem. Inf. Comput. Sci.* **2002**, *42*, 1154-1163,
[2] B3LYP-D3/6-311G**.

^{13}C Shifts of the Carbon Atoms Bound to the OH or Br in Various Alcohols and Bromides



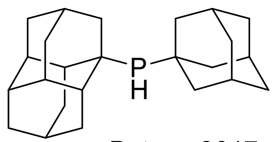
Synthesis of tri-Polymantanephospane Boranes



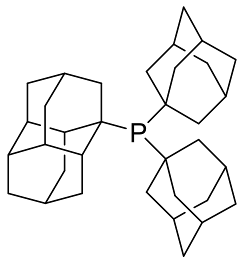
Outlook

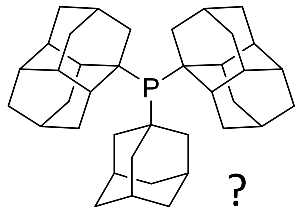
1. Diamondoid phosphines testing in palladium-catalyzed cross coupling reactions

2. Attempt to prepare 1-diamantyl substituted phosphine ligands



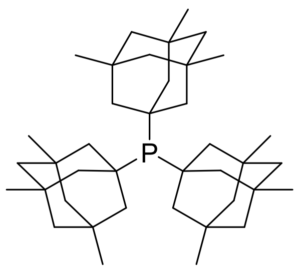
Butova 2017

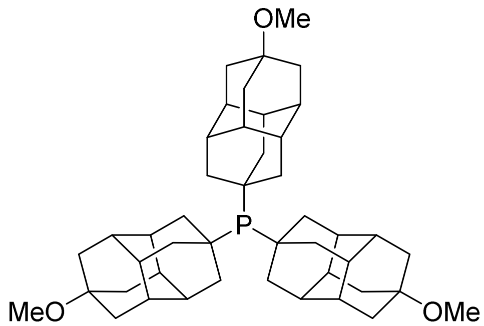




?

3. Introduction of functional groups in diamondoid phosphines





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Thank you for your attention!